REMARKS

By a Final Office Action dated January 19, 2006, the Examiner in charge of this patent application rejected the application on a variety of grounds. Based on this submission and the RCE also submitted herewith, reconsideration of the merits of this patent application is respectfully requested.

The first objection raised by the Examiner was to claim 1, the Examiner suggesting that the claimed protein be referred to as a variant of the native protein. The suggestion was appreciated, and this same nomenclature has been adopted for independent claims 9, 15 and the new claim 16 as well.

The next ground of rejection in the Office Action was under 35 USC §112, first paragraph, as containing subject matter not described in the specification. The Examiner's reasoning for this rejection was based on the argument that the claims of the present application are not based on the structural characteristics of the claimed molecules. The applicants traverse this ground of rejection. Each of the claims of this application recited clear unambiguous structural characteristics that both distinguish the prior art that are also tightly linked to the chemical phenomenon that the applicants have utilized to make improvements to ribonuclease inhibitor variants. Every claim in the application is limited by a specific amino acid change from native ribonuclease inhibitor, the substitution of a cysteine by a residue that will not form a disulfide bond. This is new to the art and a claim which distinguishes the art by a structural limitation.

First, the applicants assert that the claims do recited structural characteristics of the claimed variants. The claimed variants are defined by amino acid changes to the amino acid sequences of the claimed protein variants. In claim 1, there is specific language that recites that at least one of the paired cysteine residues in the native sequence has been substituted with another amino acid residue that cannot form a disulfide bond. In this way, the claimed proteins are explicitly claimed by reference to the structural changes that make the variant different from the native protein. While there is also functional language in the claims, that language supports the structural claim language and does not diminish it.

The Examiner stated that a human ribonuclease inhibitor according to SEQ ID NO: 3 would be allowable. To test that thesis, new claim 16 has been added. In addition, however, it is not understood how claim 15 was rejected under this grounds of rejection. This claim

claims human ribonuclease variants, all of which are exemplified in the present specification, and all of which have improved resistance to oxidation. None of the questions problems of indefiniteness cited by the Examiner on page 6 of the Office Action are applicable to this claim. It is requested that this ground of objection be reconsidered as to this claim.

The applicants still submit that the invention disclosed here has been more broadly enabled. The applicants have explained the mechanism for the change to the ribonuclease inhibitor that they have been able to cause. The applicants claim only the structural changes to the native protein sequence that result in the desired improvements. Only substitutions to paired cysteine residues have been claimed, and such substitutions are present in all ribonuclease inhibitors. The claims are appropriate in scope.

Nevertheless, in order to attempt to put the claims in condition for allowance, amendments have been made to claims 1 and 9 to further define their structural limitations.

The Examiner also again rejected the claims of this application based on the paper by Blasquez. The applicants still traverse this rejection. While Blasquez discloses that oxidation of cysteine residues is associated with its intracellular degradation of the ribonuclease inhibitor (RI), the applicants believe that nowhere does Blasquez teach making modified forms of RI for any reason.

It is acknowledged that Blasquez teaches that the disulfide bonds of RI can be oxidized. Oxidizing disulfide bonds does not involve a change of amino acid sequence in the protein, just an oxidation of the disulfide bridges between existing cysteine residues. However, the undersigned has repeatedly searched Blasquez for any teaching of modification of the amino acid sequence of native RI, and that search has been totally in vain. If the Examiner is able to find any passage in the Blasquez paper that discloses making changes the to amino acid sequence of the native protein, could he please point it out? The applicants can find no such teaching.

Without a teaching of a change to the amino acid sequence of the native ribonuclease inhibitor, Blasquez cannot anticipate the claims of this application. Every claim in this application recites that the variant which has a different amino acid sequence from the native protein sequence. The applicants believe Blasquez does not teach any change in amino acid sequence to the native RI. Accordingly, the rejection over Blasquez for anticipation is misplaced and reconsideration of this rejection is respectfully requested.

In view of these remarks, Applicants respectfully requests prompt and favourable consideration of this response and that a timely Notice of Allowance be issued in this case.

A petition for a three-month extension of time and a Request for Continuing Examination (RCE) under 37 CFR §1.114 accompany this response so the response is deemed timely filed. Please charge these fees to Deposit Account No. 17-0055. If any other fee is due or any other extension of time is required in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to the Deposit Account No. 17 0055.

Respectfully submitted,

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